

This Page Is Inserted by IFW Operations
and is not a part of the Official Record

BEST AVAILABLE IMAGES

Defective images within this document are accurate representations of the original documents submitted by the applicant.

Defects in the images may include (but are not limited to):

- BLACK BORDERS
- TEXT CUT OFF AT TOP, BOTTOM OR SIDES
- FADED TEXT
- ILLEGIBLE TEXT
- SKEWED/SLANTED IMAGES
- COLORED PHOTOS
- BLACK OR VERY BLACK AND WHITE DARK PHOTOS
- GRAY SCALE DOCUMENTS

IMAGES ARE BEST AVAILABLE COPY.

**As rescanning documents *will not* correct images,
please do not report the images to the
Image Problem Mailbox.**

Claims

1. A method of inhibiting angiogenesis in a subject in need of such treatment comprising administering to the subject at least one antiangiogenic nucleic acid molecule in an amount effective to inhibit angiogenesis in the subject.

2. The method of claim 1, wherein the at least one antiangiogenic nucleic acid molecule comprises at least one sequence set forth as SEQ ID NOs: 1-1093.

3. The method of claim 1, wherein two or more antiangiogenic nucleic acid molecules are administered.

4. The method of claim 1, further comprising administering to the subject at least one non-nucleic acid angiogenesis inhibitor molecule.

5. The method of claim 1, wherein the angiogenesis is associated with a condition selected from the group consisting of a solid tumor growth, a tumor metastasis, and a precancerous lesion.

6. The method of claim 1, wherein the nucleic acid is a CpG nucleic acid having an unmethylated CpG motif.

7. The method of claim 1, wherein the nucleic acid is a T-rich nucleic acid.

8. The method of claim 1, wherein the nucleic acid is a poly G nucleic acid.

9. The method of claim 1, wherein the nucleic acid is isolated.

10. The method of claim 1, wherein the nucleic acid does not encode a protein having antiangiogenesis activity.

11. The method of claim 1, wherein the nucleic acid has a modified backbone.

12. The method of claim 11, wherein the modified backbone is a phosphate backbone modification.

13. The method of claim 11, wherein the modified backbone is a peptide modified oligonucleotide backbone.

14. The method of claim 1, further comprising administering to the subject at least one anticancer agent.

15. The method of claim 1, further comprising administering to the subject at least one antiarthritis agent.

16. The method of claim 6, wherein the CpG nucleic acid comprises:

5' X₁ X₂CGX₃ X₄ 3'

wherein C is unmethylated, and wherein X₁X₂ and X₃X₄ are nucleotides.

17. The method of claim 16, wherein the 5' X₁ X₂CGX₃ X₄ 3' sequence is a non-palindromic sequence.

18. The method of claim 16, wherein the CpG nucleic acid has 8 to 100 nucleotides.

19. The method of claim 16, wherein X₁X₂ are nucleotides selected from the group consisting of: GpT, GpG, GpA, ApA, ApT, ApG, CpT, CpA, CpG, TpA, TpT, and TpG; and X₃X₄ are nucleotides selected from the group consisting of: TpT, CpT, ApT, TpG, ApG, CpG, TpC, ApC, CpC, TpA, ApA, and CpA.

20. The method of claim 16, wherein X₁X₂ are selected from the group consisting of GpA and GpT and X₃X₄ are TpT.

21. The method of claim 16, wherein X₁X₂ are both purines and X₃X₄ are both pyrimidines.

22. The method of claim 16, wherein X₂ is a T and X₃ is a pyrimidine.

23. The method of claim 16, wherein the CpG nucleic acid is 8 to 40 nucleotides in length.

24. The method of claim 16, wherein the CpG nucleic acid has a sequence selected from
the group consisting of SEQ ID NOs: 1, 3, 4, 14-16, 18-24, 28, 29, 33-46, 49, 50, 52-56, 58,
64-67, 69, 71, 72, 76-87, 90, 91, 93, 94, 96, 98, 102-124, 126-128, 131-133, 136-141, 146-
150, 152-153, 155-171, 173-178, 180-186, 188-198, 201, 203-214, 216-220, 223, 224, 227-
240, 242-256, 258, 260-265, 270-273, 275, 277-281, 286-287, 292, 295-296, 300, 302, 305-
307, 309-312, 314-317, 320-327, 329, 335, 337-341, 343-352, 354, 357, 361-365, 367-369,
373-376, 378-385, 388-392, 394, 395, 399, 401-404, 406-426, 429-433, 434-437, 439, 441-
443, 445, 447, 448, 450, 453-456, 460-464, 466-469, 472-475, 477, 478, 480, 483-485, 488,
489, 492, 493, 495-502, 504-505, 507-509, 511, 513-529, 532-541, 543-555, 564-566, 568-
576, 578, 580, 599, 601-605, 607-611, 613-615, 617, 619-622, 625-646, 648-650, 653-664,
666-697, 699-706, 708, 709, 711-716, 718-732, 736, 737, 739-744, 746, 747, 749-761, 763,
766-767, 769, 772-779, 781-783, 785-786, 7900792, 798-799, 804-808, 810, 815, 817, 818,
820-832, 835-846, 849-850, 855-859, 862, 865, 872, 874-877, 879-881, 883-885, 888-904,
and 909-913.

25. The method of claim 7, wherein the T-rich nucleic acid is a poly T nucleic acid
comprising

5' TTTT 3'.

26. The method of claim 25, wherein the poly T nucleic acid comprises

5' X₁ X₂TTTTX₃ X₄ 3'

wherein X₁, X₂, X₃ and X₄ are nucleotides.

27. The method of claim 25, wherein the T rich nucleic acid comprises a plurality of poly
T nucleic acid motifs.

28. The method of claim 26, wherein X₁X₂ is TT.

29. The method of claim 26, wherein X₃X₄ is TT.

30 The method of claim 26, wherein X_1X_2 is selected from the group consisting of TA, TG, TC, AT, AA, AG, AC, CT, CC, CA, CG, GT, GG, GA, and GC.

5 31. The method of claim 26, wherein X_3X_4 is selected from the group consisting of TA, TG, TC, AT, AA, AG, AC, CT, CC, CA, CG, GT, GG, GA, and GC.

32. The method of claim 25, wherein the T rich nucleic acid comprises a nucleotide composition of greater than 25% T.

10 33. The method of claim 7, wherein the T rich nucleic acid comprises a nucleotide composition of greater than 25% T.

34. The method of claim 33, wherein the T rich nucleic acid comprises a nucleotide composition of greater than 30% T.

15 35. The method of claim 33, wherein the T rich nucleic acid comprises a nucleotide composition of greater than 50% T.

20 36. The method of claim 33, wherein the T rich nucleic acid comprises a nucleotide composition of greater than 60% T.

37. The method of claim 33, wherein the T rich nucleic acid comprises a nucleotide composition of greater than 80% T.

25 38. The method of claim 7, wherein the T rich nucleic acid comprises at least 20 nucleotides.

39. The method of claim 7, wherein the T rich nucleic acid comprises at least 24 nucleotides.

30 40. The method of claim 8, wherein the poly G nucleic acid comprises:



wherein X_1 , X_2 , X_3 , and X_4 are nucleotides.

41. The method of claim 40, wherein at least one of X₃ and X₄ are a G.

42. The method of claim 40, wherein both of X₃ and X₄ are a G.

43. The method of claim 8, wherein the poly G nucleic acid comprises the following formula:



wherein N represents between 0 and 20 nucleotides.

44. The method of claim 8, wherein the poly G nucleic acid comprises the following formula:



wherein N represents between 0 and 20 nucleotides.

45. The method of claim 8, wherein the poly G nucleic acid is free of unmethylated CG dinucleotides

46. The method of claim 45, wherein the poly G nucleic acid is selected from the group consisting of SEQ ID NOs: 5, 6, 73, 215, 267-269, 276, 282, 288, 297-299, 355, 359, 386, 387, 444, 476, 531, 557-559, 733, 768, 795, 796, 914-925, 928-931, 933-936, and 938.

47. The method of claim 8, wherein the poly G nucleic acid includes at least one unmethylated CG dinucleotide.

48. The method of claim 47, wherein the poly G nucleic acid is selected from the group consisting of SEQ ID NOs: 67, 80-82, 141, 147, 148, 173, 178, 183, 185, 214, 224, 264, 265, 315, 329, 434, 435, 475, 519, 521-524, 526, 527, 535, 554, 565, 609, 628, 660, 661, 662, 725, 767, 825, 856, 857, 876, 892, 909, 926, 927, 932, and 937.

49. The method of claim 1, wherein the nucleic acid is a synthetic nucleic acid.

50. The method of claim 9, wherein the nucleic acid is administered on a routine schedule.

51. The method of claim 1, wherein the angiogenesis is associated with a condition selected from the group consisting of rheumatoid arthritis, psoriasis, diabetic retinopathy, retinopathy of prematurity, macular degeneration, corneal graft rejection, neovascular glaucoma, retrolental fibroplasia, rubeosis, Osler-Webber Syndrome, myocardial angiogenesis, plaque neovascularization, telangiectasia, hemophiliac joints, angiofibroma, wound granulation, intestinal adhesions, atherosclerosis, scleroderma, and hypertrophic scars.

52. The method of claim 1, wherein the nucleic acid is not an antisense molecule.

53. A pharmaceutical composition comprising an amount of at least one antiangiogenic nucleic acid molecule effective to inhibit angiogenesis and a pharmaceutically acceptable carrier.

54. The pharmaceutical composition of claim 53, wherein the at least one antiangiogenic nucleic acid molecule comprises at least one sequence set forth as SEQ ID NOs: 1-1093.

55. The pharmaceutical composition of claim 53, wherein two or more antiangiogenic nucleic acid molecules are administered.

56. The pharmaceutical composition of claim 53, further comprising at least one non-nucleic acid angiogenesis inhibitor molecule.

57. The pharmaceutical composition of claim 53, wherein the antiangiogenic nucleic acid molecule has a modified backbone.

58. The pharmaceutical composition of claim 57, wherein the modified backbone is a phosphate modified backbone.

59. The pharmaceutical composition of claim 58, wherein the phosphate modified backbone is a phosphorothioate modified backbone.

60. The pharmaceutical composition of claim 53, further comprising an anticancer agent.

61. The pharmaceutical composition of claim 53, wherein the nucleic acid is a CpG nucleic acid.

62. The pharmaceutical composition of claim 53, wherein the nucleic acid is a T-rich nucleic acid.

63. The pharmaceutical composition of claim 53, wherein the nucleic acid is a poly G nucleic acid.

64. The pharmaceutical composition of claim 53, wherein the nucleic acid is isolated.

65. The pharmaceutical composition of claim 53, wherein the nucleic acid is not an antisense molecule.

66. A kit comprising
a first container housing at least one antiangiogenic nucleic acid molecule, and
instructions for administering the antiangiogenic nucleic acid to a subject having a
condition characterized by unwanted angiogenesis.

67. The kit of claim 66, wherein the antiangiogenic nucleic acid has a modified backbone.

68. The kit of claim 67, wherein the modified backbone is a phosphate modified backbone.

69. The kit of claim 67, wherein the phosphate modified backbone is a phosphorothioate modified backbone.

70. The kit of claim 65, further comprising a second container housing at least one non-nucleic acid antiangiogenic agent.

71. The kit of claim 65, further comprising a second container housing at least one anticancer agent.

72. The kit of claim 69, further comprising a third container housing at least one anticancer agent.

5 73. The kit of claim 65, wherein the nucleic acid is not an antisense molecule.

74. The kit of claim 65, wherein the instructions relate to administering the antiangiogenic nucleic acid to a subject having a condition selected from the group consisting of rheumatoid arthritis, psoriasis, diabetic retinopathy, retinopathy of prematurity, macular degeneration,
10 corneal graft rejection, neovascular glaucoma, retrolental fibroplasia, rubeosis, Osler-Webber Syndrome, myocardial angiogenesis, plaque neovascularization, telangiectasia, hemophiliac joints, angiofibroma, wound granulation, intestinal adhesions, atherosclerosis, scleroderma, and hypertrophic scars.

10017995-121601